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POINT-COUNTERPOINT

To Screen or Not To Screen for Methicillin-Resistant *Staphylococcus aureus*[▽]

There are few more compelling questions in clinical microbiology today than the issue of whether or not to screen for the presence of methicillin-resistant *Staphylococcus aureus* (MRSA), with the results being used to institute infection control interventions aimed at preventing transmission of MRSA in health care environments. Numerous different matters must be addressed when considering a screening program. Who is to be screened, what method is to be employed to detect MRSA, and what sites should be sampled? When and how often should the screening be performed? Who is going to pay for the screening, and, finally and perhaps most importantly, how are screening results to be communicated to health care providers and what kind of interventions are best undertaken based on the results? Numerous governmental agencies have mandated MRSA screening programs, and yet several authorities in infection control organizations have questioned the appropriateness of mandated screening.

In this Point-Counterpoint feature, Dr. Lance Peterson of Evanston Hospital (Evanston, IL) offers his perspective on why screening for MRSA is to be encouraged. Dr. Daniel Diekema of the University of Iowa Carver College of Medicine (Iowa City, IA) offers an opposing view.

POINT

The issue as to whether or not U.S. health care organizations should aggressively deploy programs to control MRSA hinges on three critical questions. First, is the burden of MRSA disease sufficiently high so that human effort and financial resources should be directed toward this problem? If the answer is yes, then the second question is this: how do the policymakers in a health care organization decide whether MRSA is a problem for its patients? The last question, then, involves implementation: what type of MRSA control program is likely to reduce disease cost effectively?

There is considerable literature assessing MRSA disease burden across the United States. Delorme and colleagues measured the change in the incidence of *S. aureus* disease between 2006 and 2007 in northeast Ohio (2). They found an overall 77% increase in infections (59% MRSA); a 58% disease increase for outpatients, a 43% increase for hospital inpatients, and a 183% increase in residents of long-term care facilities (2). The overall burden of disease was 589/100,000 inhabitants, and for 66% of the affected persons, there were no risk factors for staphylococcal infection (2). A similar burden of disease was reported in a prevalence survey done during 2004 and 2005 in San Francisco, CA; there were 347 MRSA disease cases/100,000 population (13). To place these numbers in context, in 2007 the United States had a reported total of 13,293 tuberculosis (TB) cases, which translates to a rate of 4.4 cases/100,000 population (1); thus, the MRSA burden of disease is approximately 100-fold that of TB. Another pivotal study on MRSA was the 2005 prospective surveillance investigation of invasive disease reported by Klevens and colleagues, who found that 77% of MRSA health care-associated infections consisted of cases of bacteremia—a doubling in 6 years (12). They discovered a disease rate of 31.8/100,000 population, with an annual mortality of 20% (18,650 deaths), representing more deaths than those due to HIV-AIDS (12). If one assumes that a disease burden 100-fold higher than that of TB and with an annual mortality rate exceeding that of HIV-AIDS is a significant illness for the United States, then the answer to the first question is yes.

The response to the second question is also straightforward. The Joint Commission requires infection control personnel at each health care organization to perform an annual risk assessment to determine the key health problems (22). For MRSA, as well as for any multidrug-resistant organism, the Centers for Disease Control and Prevention (CDC) recommend that all health care organizations assess their rate of multidrug-resistant organism infections and demonstrate that the rate is actually diminishing over time or, if not, to implement additional (Tier 2) disease control measures (20). One of the most important Tier 2 measures is active surveillance (20). For a laboratory to assist in this assessment, one appropriate approach is to determine the number of organisms (e.g., MRSA) recovered from clinical specimens and to track the change in the rate

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(per 1,000 admissions or 1,000 patient days) over time. While this method may detect some colonization as well as disease, such an approach has been shown to accurately identify 77.1% of actual *S. aureus* infections (5) and to provide significant changes in disease rates much faster than when only bacteremia rates are measured (24). Another useful tool to assess MRSA risk for patients is to perform a point prevalence survey for MRSA (nasal) colonization. We found this undertaking enlightening for both infection control and senior management when 8.5% of our inpatients showed nasal MRSA colonization (18), a rate which was some threefold higher than the 2.7% reported by Jernigan and colleagues from an admission MRSA prevalence survey done 6 years earlier (10). These data led to institution-wide recognition that there was a high level of MRSA colonization in our patient population and facilitated deployment of an aggressive MRSA control program. Once a local problem has been shown to exist, the next step is to design an intervention that is likely to succeed in lowering MRSA infection—remembering that the most expensive program, no matter how much or how little is done, is one that does not reduce MRSA disease.

A key to reducing MRSA dissemination and subsequent disease is the need to enhance practices that reduce spread; those practices are currently considered to be barrier precautions or contact isolation. Figure 1 illustrates how this can be effective. In each pictured scenario, there is a constant influx of new MRSA carriers (due to person-to-person spread); in the first scenario (Fig. 1A), the rates of both colonization and eventual disease rise until a higher plateau is reached. Only when 90% of disease spread has been blocked (as illustrated in the third scenario [Fig. 1C]) are there actual reductions in both colonization and infection. The required level of detection (via surveillance through screening for MRSA) to reduce MRSA spread varies with the prevalence of colonization and disease. For any given MRSA prevalence rate, the factor that seems most crucial in reducing spread is the percentage of potential isolation days captured for patients admitted who are infected or colonized with this pathogen. The influential operational processes are (i) the sensitivity of the screening test, (ii) the speed with which newly detected positive patients are reported to the nursing unit (assuming that preemptive isolation is not employed), and (iii) the selection of patient population(s) who are to undergo surveillance.

The utility of various testing approaches for MRSA surveillance has recently been investigated by meta-analysis (21), and the conclusion of the authors was that surveillance for MRSA colonization was beneficial in reducing disease. However, they also concluded that rapid testing had not been proven to be superior to culture-based methods. A lapse in their analysis was that

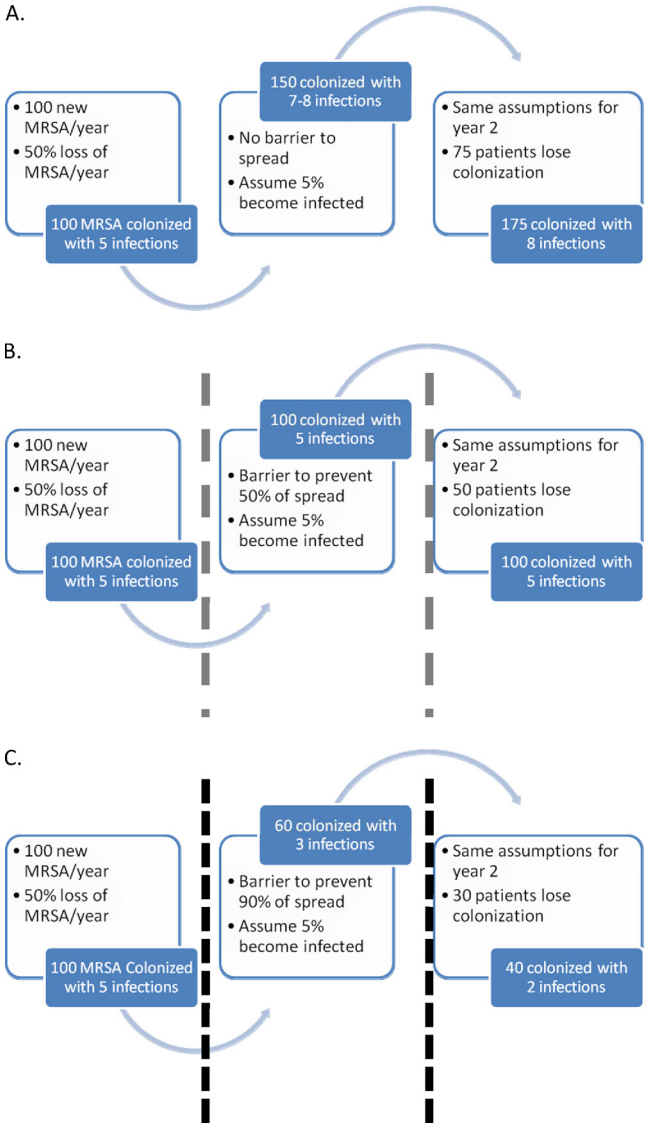

FIG. 1. Representation of the impact of barriers (contact isolation) on MRSA. Each "boxed" segment represents 1 year of time, with panels A, B, and C representing three levels of effective barrier precautions (no prevention of spread, 50% prevention, and 90% prevention).

the authors did not investigate the effect of the levels of sensitivity and speed of reporting on the success or failure of MRSA control programs in the reviewed articles (21). Several recent publications give insights into this critical aspect of laboratory practice when dealing with a population with modest (5 to 7%) MRSA colonization prevalence (6, 7, 8, 11, 19). In a report by Robicsek and colleagues, the authors suggest that the capture of potential MRSA isolation days has the greatest effect on whether or not a MRSA control program exerts a significant impact on disease reduction (19). They reported that admissions policies that omitted active MRSA surveillance (capturing only those persons who had given MRSA-positive results in the past) placed admitted pa-

TABLE 1. Summary of published reports that illustrate the impact of different levels of test sensitivity and time to reporting of results on the reduction of MRSA in the involved population

Report authors (reference)	% MRSA prevalence	Mean length of hospital stay (days)	% Test sensitivity	Time to result report (h)	Length of intervention period (mo)	Estimated MRSA isolation days captured (%)	Success of program in reducing MRSA disease
Harbarth et al. (7)	6.7	3.7 to 4	84	≥22.2	5 to 17	63	No reduction in disease
Harbarth et al. (6)	5.1	6.4	84	≥22 to 23	9	72	No reduction in disease
Robicsek et al. (18)	6.3	4.6	98	15	21	85	Reduction in disease with universal surveillance[a]
Jeyaratnam et al. (11)	6.7	3.8	87.8	≥22	5	67	No reduction in transmission or disease
Hardy et al. (8)	6.3	7.2	98[b]	22	8	86	Reduction in transmission[a]
Hardy et al. (8)	5.2	6.5	≤73	42 (direct culture)	8	53	No reduction in transmission

[a] Results represented statistically significant reductions.
[b] Sensitivity data were calculated based on the methods presented in reference 14.

tients into appropriate isolation for approximately 18% of their inpatient days and that adding active surveillance for intensive care unit (ICU)-admitted patients increased that to 33% of inpatient days, with neither approach having any impact on MRSA disease control over sequential 12-month periods of time (19). Only when all admission active surveillance was implemented using a test that was 98% sensitive and had a reporting time of ≤15 h was there capture of 85% of potential inpatient MRSA isolation days; this led to a significant (>70%) reduction in MRSA infection (19).

The relevant articles and important characteristics leading to the estimation of captured MRSA isolation days are presented in Table 1. For each of these reports, one can calculate the approximate percentage of captured potential MRSA isolation days based on test sensitivity, time to reporting, and length of hospital stay. As can be seen in these reports, no success was recognized in reduction of either MRSA transmission or infection during the relatively brief intervention periods until the estimated captured MRSA isolation days exceeded 80%. Thus, it appears that if a relatively short period of time (<1 year) is used to evaluate a MRSA control program, then a very aggressive, broadly directed surveillance program is required. Importantly for the laboratory, the shorter reporting time and lower sensitivity of culture for MRSA detection can influence the percentage MRSA isolation days captured (15), which implies that the actual assay selection is critical to the outcome of any intervention and that only a rapid test with high sensitivity may provide a satisfactory programmatic result.

While there has been success in lowering the incidence of MRSA disease without the use of active surveillance, these interventions have been in the setting of very high infection prevalence. For example, Grayson and colleagues reported on the reduction of the rate of recovery of monthly MRSA clinical isolates by their laboratory from 1.39 to 0.73 per 100 discharges, a change which was considered to have been associated with an improvement of hand hygiene compliance from 21% to 48% over 2 years (4). Monthly bacteremia rates also fell from 0.05 to 0.02 per 100 discharges (4). Similarly, Edmond and colleagues reported a significant reduction in device-related MRSA infection from 2.9 to 0.76 infections per 1,000 patient-days over 4 years of multiple interventions (3). However, the ending infection rates for both studies at the conclusion of their interventions were higher than the initial disease rate found by Robicsek et al. (19), suggesting that in a very high prevalence setting nearly any intervention can be beneficial but that at some point active surveillance must be undertaken. In support of this concept, Huang and colleagues reported on sequential ICU interventions aimed at lowering MRSA blood stream infection rates (9). They serially introduced maximally sterile central venous catheter placement, an alcohol hand rub, a hand hygiene campaign, and ICU MRSA surveillance; the only intervention that had a sustained impact on lowering the incidence of MRSA bacteremia was active surveillance (9).

Finally, there is the question of cost-effectiveness for any program designed to reduce the spread of MRSA colonization and disease. As noted earlier, the program that is most costly in human and financial resources is one that has no measurable beneficial impact over the time allotted for assessment. We have previously reported using a very conservative model that each patient developing a health care-associated MRSA infection has an excess medical cost of nearly $24,000 (18). On 31 July 2009, we completed the first 4 years of our MRSA program at NorthShore University HealthSystem; by that time, there had been (compared to baseline) 406 MRSA infections avoided, with an $8.8 million excess that had not needed to be spent for this preventable illness (17). Importantly, using the mortality estimate of Klevens and colleagues (12), we had avoided 72 deaths from invasive MRSA disease (17).

In conclusion, the available data indicate that MRSA infection is a serious health risk for the U.S. population. It is also likely that MRSA infection is a problem for most health care organizations and that assessing that

risk can be done with minimal time and financial resources. Finally, active surveillance for this pathogen can reduce disease, both locally and nationally (19, 23). Arguments against such programs for MRSA control typically hinge on statistical methods and adverse effects of isolation and focus on a single problem, but these concerns stand on very little evidence (16). The appropriate prevention and control of MRSA colonization and disease remains achievable, saves lives, and is cost-beneficial.

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COUNTERPOINT

I begin by emphasizing two points upon which Dr. Peterson and I agree. First, methicillin-resistant *Staphylococcus aureus* (MRSA) is an important cause of morbidity and mortality and should be a focus of infection prevention efforts. Second, there is a role for "active detection and isolation" (ADI) in the control of multidrug-resistant organisms (MDROs), including MRSA. As outlined by the Centers for Disease Control and Prevention guidelines, ADI is one of several "second tier" interventions that should be considered when "first tier" infection prevention measures fail to prevent MDRO transmission (e.g. during outbreaks) (16).

The question I will address is whether universal ADI should be implemented as a routine MRSA infection prevention measure. In other words, should all hospitals screen newly admitted patients for MRSA? My answer to this question is no, for the reasons I outline below.

The effectiveness of ADI remains in question. The effectiveness of ADI for MRSA infection prevention has been argued *ad nauseam* in the infection control literature, so in the interest of conserving space I refer the reader to two recent systematic reviews (2, 13), to the CDC MDRO guidelines (16), and to a joint statement issued by the two major U.S. infection prevention professional societies (the Society for Healthcare Epidemiology of America and the Association for Professionals in Infection Control) (19). These publications summarize the state of the literature on ADI for MRSA control and present conclusions indicating that the existing evidence is not strong enough to support adoption of MRSA ADI as a routine infection prevention measure. Why? Because almost all the published studies are of limited quality, in most cases due to an observational, before-and-after study design, the absence of concurrent control groups, and the inclusion of multiple interventions, making it difficult to determine the contribution of ADI to the observed MRSA reductions (2, 13). For example, the most widely cited recent study of universal ADI lacked a control group and included interventions other than ADI (e.g., widespread decolonization) (15). By contrast, the largest-ever controlled trial of universal ADI to reduce MRSA infections demonstrated no difference in MRSA infection rates associated with ADI use (8).

ADI interventions are complex and resource intensive. The reader is referred to our more comprehensive guidance for details (3), but in brief, the implementation of ADI is a resource-intensive, multidisciplinary effort. In addition to the cost of the screening test itself (up to $25 to $45 per test for the commercial PCR tests), there are costs associated with sample acquisition and transport, laboratory validation and reporting, process and outcome monitoring, personal protective equipment, bed management, and patient/family education (3). The argument that these costs are offset by savings from MRSA infection prevention assumes that MRSA infections cannot be prevented using measures other than ADI—a flawed assumption.

Importantly, the resources invested in MRSA ADI are designed to prevent only MRSA infections. Indeed, MRSA ADI papers frequently cite the failure of MRSA ADI to impact non-MRSA infection rates as evidence in support of the specificity of the intervention (15). Infection prevention programs obviously must focus on several problems at once. However, resources are not infinite, and every dollar spent on an MRSA-specific ADI intervention is a dollar not available for population-based interventions designed to prevent both MRSA and all other health care-associated infections (20).

ADI may have unintended adverse consequences. A premise of ADI is that there are many asymptomatic carriers of MRSA, each of whom serves as a reservoir for nosocomial transmission unless detected and placed in isolation. Therefore, any comprehensive ADI program will significantly increase the number of patients being cared for under conditions of contact precautions (3). Unfortunately, several studies have demonstrated adverse consequences for patients under those conditions, including fewer health care worker visits, more noninfectious adverse events (missed medication doses, falls, decubitus ulcers, electrolyte disorders), more depression and anxiety, and lower satisfaction with hospital care (14, 17).

While it may be possible for some hospitals to implement ADI and protect patients from unintended adverse consequences of contact precautions, there is an urgent need for more research in this area. A limitation of the ADI literature is that it focuses narrowly on infection outcomes and ignores noninfectious adverse outcomes and overall patient satisfaction with respect to care (3, 5).

Given its uncertain effectiveness, the potential for harm, and the existence of alternative interventions for MRSA prevention, it is appropriate to examine the ethical implications of implementing universal MRSA ADI. Due to space limitations, the reader is referred to a previously published detailed ethical assessment of ADI for MDRO prevention (5).

ADI is not necessary for MRSA prevention. The strongest argument against routine, universal ADI is that it is not necessary for MRSA prevention. Several hospitals have reported significant reductions in MRSA infection or transmission by the use of approaches that do not include ADI (4, 9, 12). While these studies share the flaws of studies supporting MRSA ADI (e.g., before-after design and absence of control groups), the MRSA outcome reductions have been of similar or greater magnitude (see Table 1). For example, the most recent such report presents findings showing a 73% reduction in device-associated MRSA infection rates in all adult intensive care units over a 4-year period and indicates that the reduction was associated with broad-based infection control strategies (e.g. hand hygiene and implementation of bundled interventions to reduce device-associated infections) (4). This hospital, after adding chlorhexidine body washes for all ICU patients, has more recently reported even greater reductions in MRSA infection rates (6). In the medical ICU of my own hospital, we are entering our fifth consecutive month with no device-associated infections of any kind, MRSA or other. We attribute this success to sustained hand hygiene adherence of 70 to 90% and bundled interventions

TABLE 1. Examples of declining MRSA infection rates without the use of universal ADI[a]

Study design or surveillance program	Setting and dates	Major interventions	Outcome measure(s)	% Decrease(s) in MRSA endpoint	Reference(s)
Single center					
Before-and-after	Adult ICUs, 820-bed hospital in Virginia, 2003–2009	Hand hygiene, unit-level S&F, CLABSI/VAP, bundled interventions, chlorhexidine baths	Device-associated MRSA infection rates	By 2006, 73 (pooled); By 2009, 91 (CLABSI) (94% VAP, 71% UTI)	4, 6
Before-and-after	840-bed hospital, Australia, 2001–2004	Hand hygiene, environmental cleaning, "culture change"	MRSA bacteremia	57	12
Before-and-after	350-bed hospital, Australia, 2003–2006	Hand hygiene, unit-level S&F	New MRSA isolation, MRSA bacteremia	43, 40[b]	9
National					
United Kingdom National Health Service (HPA)[c]	United Kingdom hospitals, 2007–2009	Public reporting; various[d]	MRSA bacteremia	57	10
NNIS and NHSN	U.S. ICUs, 1997–2007	Various[d]	MRSA CLABSI	50	1
EARRS	Europe, 1998–2008	Various[d]	Proportion of MRSA among invasive *S. aureus* bacteria	In 9 countries, significant decrease over previous 4 years (versus 2 countries with an increase)	7

[a] S&F, surveillance and feedback of infection rates to each unit; CLABSI, central line-associated bloodstream infection; VAP, ventilator-associated pneumonia; UTI, urinary tract infection; HPA, Health Protection Agency; NNIS, National Nosocomial Infection Surveillance System; NHSN, National Healthcare Safety Network; EARSS, European Antimicrobial Resistance Surveillance System.
[b] Values refer to percent decrease in new MRSA isolation and MRSA bacteremia, respectively.
[c] The Health Protection Agency in the United Kingdom has mandated reporting of MRSA bloodstream infection since 2001.
[d] Universal ADI was not practiced across these surveillance programs. Because each program represents hundreds of hospitals, it is not possible to list all interventions that were performed.

to prevent device-associated infections. We do not practice MRSA ADI.

In addition to individual hospital reports of reductions of rates of MRSA infection without ADI, there are several lines of evidence indicating that health care-associated MRSA infection rates are declining as increased attention is paid to basic hospital infection prevention. Catheter-associated bloodstream infections due to MRSA have declined by over 50% in U.S. ICUs since 2001 without widespread use of ADI (1). The United Kingdom successfully reduced MRSA bloodstream infections by 57% from 2007 to 2009 without adoption of universal ADI (a mandatory ADI program for elective admissions was not introduced in the United Kingdom until April 2009) (10). Finally, the European Antimicrobial Resistance Surveillance System now has more countries with decreasing trends in MRSA rates as opposed to increasing trends, and most participating countries do not perform universal MRSA ADI (7).

ADI is a flawed infection prevention approach. Infection prevention practices are designed to prevent patients from becoming infected with their own flora or with flora from other persons or the hospital environment. This applies to all potential microbial pathogens and not just MRSA. Universal ADI interventions assume that we cannot prevent MRSA infections without knowing exactly who carries the organism. If this is to be our new paradigm—that MDRO infections can be prevented only if we know who carries each MDRO—then the path ahead will be extremely difficult. For as much attention as MRSA receives, it accounts for only 8% of all health care-associated bacterial infections in the United States (11) and only 10% of ICU infections worldwide (18). What organisms make up the remaining 90%? Among them are a stunning array of multiply resistant Gram-negative rods. Compared with the emerging multiply resistant Gram-negative rods, MRSA is a relatively simple pathogen—one major resistance mechanism and one gene (*mecA*) to detect, with abundant data on human carriage patterns available. Applying ADI to multiply resistant *Acinetobacter*, *Pseudomonas*, and *Stenotrophomonas* organisms, and to the multiplicity of extended-spectrum-beta-lactamase and carbapenemase producers, will be a much greater challenge.

Alternatively, we could devote our full attention, and our resources, to strengthening broad-based infection prevention programs designed to eliminate all health care-associated bacterial infections, those due to MRSA included (20).

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SUMMARY

In this Point-Counterpoint feature, Dr. Peterson presents a compelling case in favor of active, broad-based, patient-directed surveillance of both colonization and infection with MRSA linked to aggressive infection control intervention as a means of reducing the burden of MRSA disease in acute care hospitals. He cites the results of three published studies (Robicsek et al., Harrington et al., and Huang et al.) as supporting a comprehensive screening program and argues that such screening can result in lower MRSA infection rates and institutional cost savings. Dr. Peterson emphasizes the need for using molecular methods characterized by high detection sensitivity and same-day provision of test results when screening for MRSA and asserts that only when ≥90% of transmission is blocked can there be a meaningful reduction is infection rates. He also elucidates the concept of "captured MRSA isolation days" and points out that only when this value exceeds 80% can an MRSA screening program be expected to have a measurable positive impact.

Dr. Diekema presents an equally compelling case for not performing routine comprehensive MRSA surveillance. First, Dr. Diekema elucidates many of the design shortcomings in the studies used to justify MRSA screening linked to infection control interventions. He also points out that in the largest published study to date assessing the value of MRSA screening, no impact on infection rates was observed. He states that two major concerns with any comprehensive MRSA screening program are the associated costs, some of which are hidden and therefore often not taken into account when performing economic analyses, and the increase in numbers of patients being cared for under conditions of contact precautions, with the resulting potentially negative impact of these precautions on patient care and patient well-being. And finally and importantly, Dr. Diekema makes the point, based on three published studies, that decreases in MRSA infection rates can be achieved using methods other than comprehensive MRSA surveillance (Edmond et al., Harrington et al., Johnson et al.).

I would like to thank both Lance Peterson and Daniel Diekema for their most insightful discussions of this very complex matter. The fact that two experienced authorities in this area can have such different views underscores the complex nature of the many issues surrounding MRSA screening. Their commentaries provide an important platform for further discussion, debate, and study of those factors that can lead to a reasoned and coherent approach for decreasing the burden of MRSA infections.

Gary V. Doern
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The views expressed in this feature do not necessarily represent the views of the journal or of ASM.